Acute Cholangitis

Multivariate Analysis of Risk Factors

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In order to identify risk factors in patients with acute cholangitis, 140 clinical, biochemical, etiologic, and pathologic variables of 449 attacks of acute cholangitis seen in one center over a 20-year period were analyzed. Simple regression revealed 24 factors with prognostic significance, but multivariate analysis detected only seven factors with independent significance in predicting mortality (acute renal failure, cholangitis associated with liver abscesses or liver cirrhosis, cholangitis secondary to high malignant biliary strictures or after percutaneous transhepatic cholangiography, female gender, and age). When the presence of each of these factors is weighted proportional to its coefficient of regression, patients with cholangitis could be scored on a scale of 0–27. A score of seven was clinically the most useful cut off—388 attacks of cholangitis associated with a score of < 7 had a mortality rate of only 1.8%, whereas 61 attacks associated with a score ≥ 7 had a mortality rate of 49%. The value of this scoring system needs to be confirmed in prospective studies, but it may prove useful, for example, in selecting a group of high-risk patients for urgent biliary decompression in an attempt to reduce the mortality associated with this pathology.

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MULTIFACTOR PROGNOSTIC scoring systems using clinical, biochemical, and hematologic indicators are well-established in the management of acute pancreatitis.[1,2] They can be used to select a group of high-risk patients soon after admission to hospital (when the outcome of the disease is difficult to predict on clinical impression alone) for more vigorous monitoring and aggressive treatments that would not be applicable in the majority of patients with mild disease.

Acute cholangitis is a disease with a spectrum of severity similar to that of acute pancreatitis. Many patients with cholangitis receive antibiotic therapy alone,[3,4] whereas others will develop severe suppurative or obstructive cholangitis requiring urgent decompression of the biliary tree and associated with a mortality of 13–88%.[4–12] It is not always clinically apparent which patients will respond to medical treatment alone and which will require biliary decompression. The mortality rate is high for patients who undergo delayed biliary decompression after failure of medical therapy.

In the literature, there is a paucity of prognostic factors determined for acute cholangitis. This study was undertaken to identify factors useful in predicting mortality at an early stage in the disease process, with a view to identifying a high-risk group of patients who might be selected for urgent decompression of the biliary tree.

Patients and Methods

A retrospective analysis of the clinical notes for all patients treated at Paul Brousse hospital for acute cholangitis during the period 1963–1983 was performed. To qualify for inclusion in the study, patients had to present a clinical picture of cholestasis and infection with positive blood and/or bile culture and an anomaly—usually an obstruction—of the biliary tract.

One hundred and forty clinical, biologic, etiologic, and pathologic variables were analyzed against hospital mortality rate; the principle variables are shown in Table 1. Data were stored and analyzed on an IBM™ computer using the chi square test or Student's t-test. A p value of > 0.05 was considered statistically significant. Multivariate analysis was done by stepwise logistic regression.

Results

Four hundred and forty-nine attacks of acute cholangitis in 412 patients were analyzed. The mean age of the

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TABLE 1. *Principal Variables*

Clinical	Age, sex, previous biliary history, pain, fever, rigors, jaundice, shock, neurologic signs, renal failure, gastrointestinal hemorrhage, liver abscess, hepatomegaly, abdominal tenderness, suppuration in the biliary tract, Reynold's Pentad,[13] Charcot's Triad[14]
Biologic	WCC, bilirubin, SGOT, SGPT, gamma GT, alkaline phosphatase, amylase, creatinine, urea, blood and bile culture results, number and type of organism
Etiologic	Causes sites and degrees of biliary abnormality
Pathologic	Associated pathologies (*e.g.*, liver cirrhosis, liver abscesses, metastatic liver disease), O'Connor's grade of cholangitis[12]
Treatment	Type (medical/surgical/endoscopic/percutaneous) timing, antibiotics used, clinical response, dialysis.

SGOT = serum glutamic oxaloacetic transaminase.
SGPT = serum glutamic pyruvic transaminase.

patients was 58 years; 54% of the patients were older than 60 years of age, whereas 31% were older than 70 years of age. Fifty-eight per cent of the patients were women. Sixty-one per cent of patients had undergone previous biliary tract surgery, and 10% had liver cirrhosis. The etiology of the attacks is given in Table 2, and the bacteriology is shown in Table 3. The overall mortality rate was 8.2%. Sixty-three attacks were treated medically only (mortality rate of 16%), 353 attacks were treated by surgical biliary decompression (mortality rate of 6.5%), and 33 patients underwent nonsurgical decompression of the biliary tract (mortality rate of 12%).

Simple regression revealed 24 factors significantly associated with mortality (Table 4). It is interesting to note that Reynold's pentad[13] (fever, jaundice, abdominal pain, shock, and abnormal mental status) was involved in only 3.5% of attacks, but was associated significantly with mortality, whereas Charcot's original triad[14] (fever, jaundice, and abdominal pain) was involved in 72% of attacks and was not significantly associated with mortality.

Multivariate analysis demonstrated seven factors with independent significance in predicting mortality (Table 5). The logistic regression equation for estimating the probability of mortality is shown in Table 6.

This equation can be used to provide a prognostic score for individual attacks of cholangitis on a scale of 0–27. Mortality is related in a linear fashion to the score (Table 7). For each score, the Index of Youden was calculated.

TABLE 2. *The Etiology of the Attacks of Acute Cholangitis*

Etiology	Incidence
Lithiasis	48%
Common bile duct	44%
Intrahepatic	4%
Benign strictures	28%
Malignant strictures	11%
High	7%
Low	4%
Sclerosing cholangitis	1.5%
Caroli's disease	0.7%
Radiologic	5.5%
PTC	3.8%
Others	1.7%
Others/unknown	5.3%

PTC = percutaneous transhepatic cholangiography.

TABLE 3. *Bacteriology*

	Bile Culture	Blood Culture
Bacterial detection	99%	29%
Single bacteria	44%	77%
Multiple bacteria	56%	23%
Escherichia coli	35%	53%
Enterococcus	16%	8.7%
Klebsiella	14%	11%
Proteus	12.5%	6%
Pseudomonas	9%	9%
Enterobacter	5%	5%
Aerobacter	3.4%	0.7%
Staphylococcus aureus	1.4%	3.4%
Anaerobes	0.9%	2%
Candida	0.9%	0.7%

TABLE 4. *24 Factors Showing Ability to Predict Mortality Using Simple Regression*

Factor	Characteristic	Incidence	Mortality (p-value)
Clinical	Age ≥ 50 years	69.5%	<0.05
	Pus in the biliary tree	6.7%	<0.001
	Septic shock	7.8%	<0.001
	Neurologic signs	7.0%	<0.001
	Acute renal failure	9.6%	<0.001
	Associated liver abscesses	5.3%	<0.001
	Gastrointestinal hemorrhage	3.8%	<0.001
	Hepatomegaly	26.7%	<0.001
	Peritonitis	4.6%	<0.001
	Reynolds pentad[13]	3.5%	<0.001
Biologic	WCC > 10×10^9/L	79%	<0.005
	Bilirubin > 4 mg %	68%	<0.05
	Raised alkaline phosphatase	93%	<0.05
	Urea > 80 mg % or creatinine > 2 mg %	28.5%	<0.005
	Positive blood culture	29%	<0.005
	Multiple organisms in the bile	56%	<0.01
Etiologic	Malignant biliary stricture	11%	<0.001
	Radiologic—post-PTC	3.8%	<0.001
	Sclerosing cholangitis	1.5%	<0.05
	Caroli's disease	0.7%	<0.001
Pathologic	Non-biliary liver cirrhosis	4.9%	<0.001
	O'Connor's Grade III cholangitis[12]	7%	<0.001
	Liver abscesses	5.9%	<0.001
	Liver metastases	0.7%	<0.001

TABLE 5. *Multivariate Analysis of Prognostic Factors for Mortality*

Variable	Regression Coefficient	Standard Error	p-value
Acute renal failure	0.401	0.038	<0.001
Associated liver abscesses	0.312	0.048	<0.001
High malignant biliary stricture	0.242	0.061	<0.001
Liver cirrhosis	0.173	0.052	<0.001
Radiologic cholangitis—post-PTC	0.112	0.024	<0.05
Female sex	0.045	0.019	<0.05
Age (≥50 years)	0.0012	0.0006	<0.05

A score a seven appears to be the clinically useful cut-off. Three hundred and eighty-eight attacks associated with a score of < 7 resulted in a mortality rate of 1.8 %, whereas 61 attacks associated with a score ≥ 7 resulted in a mortality rate of 49% ($p < 0.001$) (Fig. 1). Using this cut-off, the scoring system has a sensitivity of 81% and a specificity of 92% in predicting mortality, and 91.5% of attacks were correctly predicted.

The study confirmed the importance of the initial response to antibiotic therapy. Attacks that responded immediately to antibiotic therapy (n = 389) were associated with a mortality of 1.5%, whereas attacks that did not respond (n = 60) were associated with a mortality of 62% ($p < 0.01$). The same significant difference occurred regardless of whether the subsequent biliary decompression was surgical or nonsurgical. The same was also true for the 61 attacks predicted as being severe through the use of the scoring system (scores ≥ 7); those attacks that responded to initial medical therapy (n = 27) were associated with a mortality of 14%, whereas those that did not (n = 33) were associated with a mortality rate of 76% ($p < 0.01$).

Discussion

Several attempts have been made to define clinical and laboratory criteria identifying a high-risk group of patients undergoing biliary surgery,[15-17] but few studies have looked specifically at patients with cholangitis. In one study of 94 patients with cholangitis in which 14 clinical and biochemical variables were analyzed, serum albumin concentration was significantly lower and serum urea concentration was significantly higher in patients who died. When only those patients with gallstone etiology were considered, serum creatinine concentration was also higher in patients who subsequently died than in survivors.[18]

Williamson[19] suggested three reasons for separating patients with acute pancreatitis into groups based on whether their prognosis was good or bad on admission:

1) The severe group need more vigorous resuscitation and monitoring, including intensive care facilities, urethral catheterization, and central venous monitoring. This would be costly if applied to all patients.

TABLE 6. *Logistic Regression Equation for Estimating the Probability of Mortality*

	Dummy Variable	Scoring System (×20)
Mortality =		
+0.401 X acute renal failure	+	8
+0.312 X associated liver abscesses	+	6
+0.242 X high malignant biliary stricture	+	5
+0.173 X associated liver cirrhosis	+	4
+0.112 X radiologic cholangitis—post-PTC	+	2
+0.045 X female sex	+	1
+0.0012 X age (≥50 years)	−	1
+0.046		0–27 (the score for each patient)

TABLE 7. *Predictive Value of the Scoring System*

Score	Mortality ($p < 0.01$)	Standard Error
0 (n = 40)	0%	0%
1–5 (n = 332)	1.8%	0.7%
6–10 (n = 53)	21%	5%
11–15 (n = 12)	67%	13%
>15 (n = 12)	100%	0%

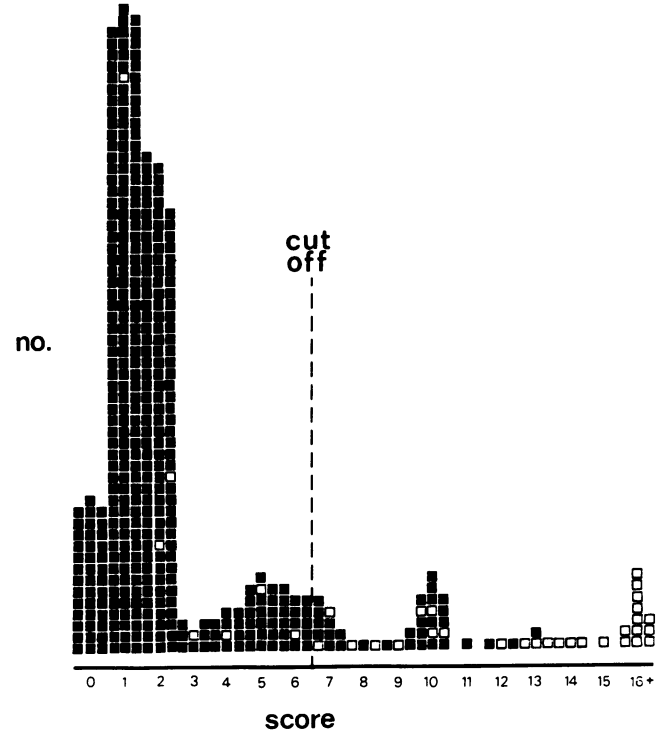

FIG. 1. Histogram of prognostic scores showing clinically useful cut-off point.
Survivors = ■.
Deaths = □.

2) Aggressive treatment such as early surgery might be justified in patients with a poor outlook, but not in the majority of patients with a mild attack, which would quickly abort when the patient received medical treatment.

3) General acceptance of criteria of severity facilitates international comparisons for prospective studies.

These arguments hold equally well for acute cholangitis, which has a similar spectrum of severity.

Prognostic scoring systems based on clinical and laboratory criteria recorded soon after admission[1,2] have gained wide acceptance in the management of acute pancreatitis in which the outcome is notoriously difficult to predict from early clinical impression alone. The predictive value of the various systems is generally reported to be within the range of 70–90%. A similar scoring system may be of value in treating acute cholangitis because the outcome is also often difficult to predict on initial clinical impression alone.

In the present study, we used multivariate analysis to reduce the number of identified risk factors to seven, all having independent significance in predicting mortality. Weighting each factor according to its discriminant function is more complex than giving a single point for each adverse factor present, but produces a higher sensitivity and specificity for the prediction of mortality and an overall predictive value of 91.5%.

The value of such a system in identifying high-risk patients needs to be confirmed in further studies. We plan a retrospective study for patients seen during the years 1984–1988 as well as a prospective study in which the score can be compared with initial clinical assessment of severity. The specialist referral pattern to the hepatobiliary unit at Paul Brousse hospital is reflected in the fact that 61% of our patients had undergone previous biliary surgery and that 10% had liver cirrhosis. It remains to be seen whether the predictive value of the scoring system will be as high in a nonselected group of patients as that which might be seen in a typical general hospital, where a higher proportion of cholangitis will be associated with calculi and fewer patients will have undergone previous biliary surgery.

Should the predictive value of the scoring system be confirmed, we would advocate its use in all three of the categories suggested by Williamson.[12] In addition to intensive rescuscitation and monitoring, the high-risk group of patients identified in this study (46% mortality for score of ≥ 7) might in the future benefit from aggressive treatment protocols; the mortality in this group of patients rose to 76% when there was no response to initial medical therapy.

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